CBER Compliance Update

Tenth Annual Surviving the Challenges of FDA and Other Regulatory Authorities' GMPs
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Basel, Switzerland

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CBER Compliance Update

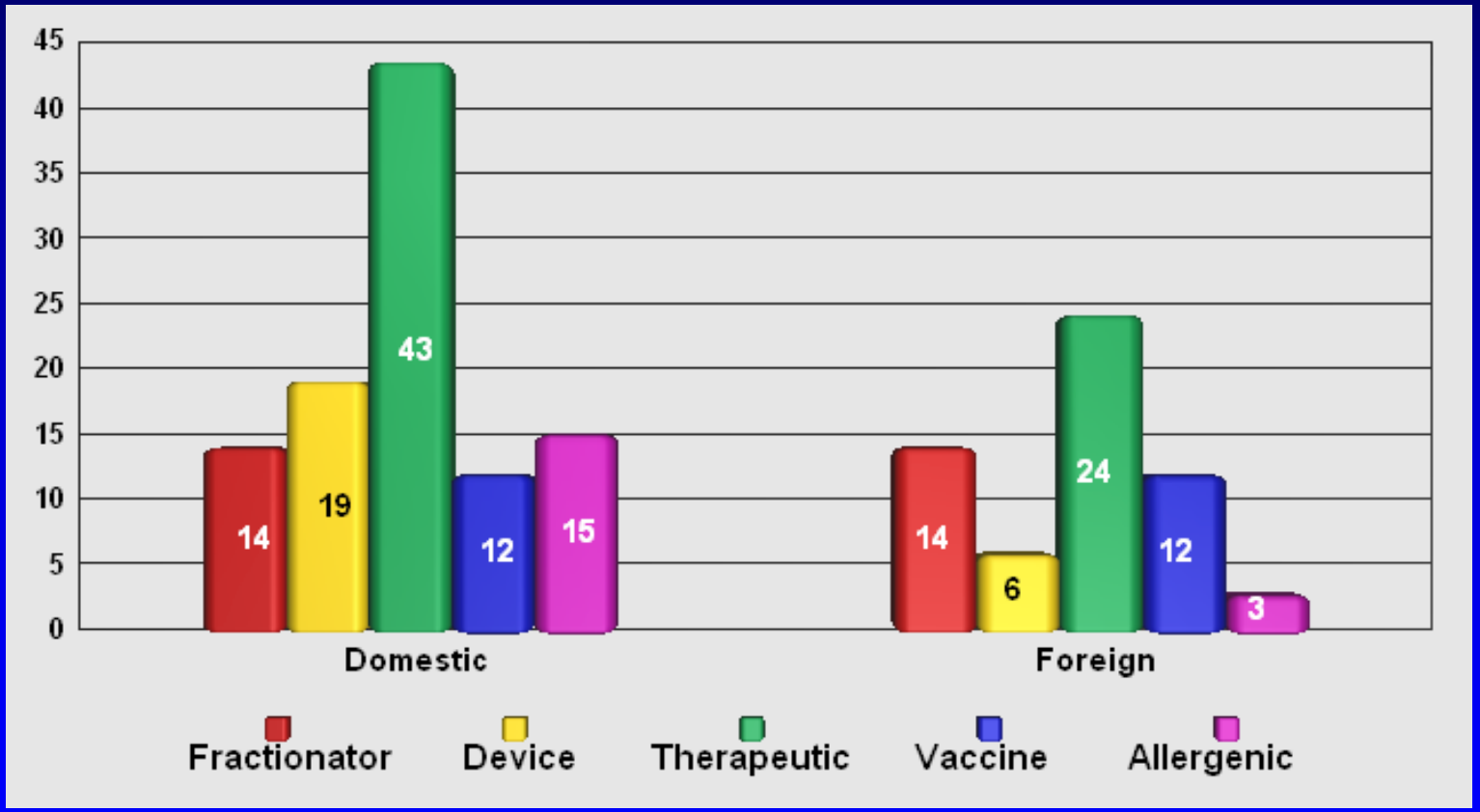
- Compliance Actions
- Import Alerts
- Bioresearch Monitoring
- NIDPOE Citations
- Anti-Counterfeiting Efforts

Compliance Actions

- **Inspection Data**
- **Warning Letters**
- **Notice of Intent to Revoke**
- **Injunctions**
- **Recalls**
- **Import Alerts/Import Detentions**

FDA Inspection Inventory*

Biologics



* As of 1/20/04

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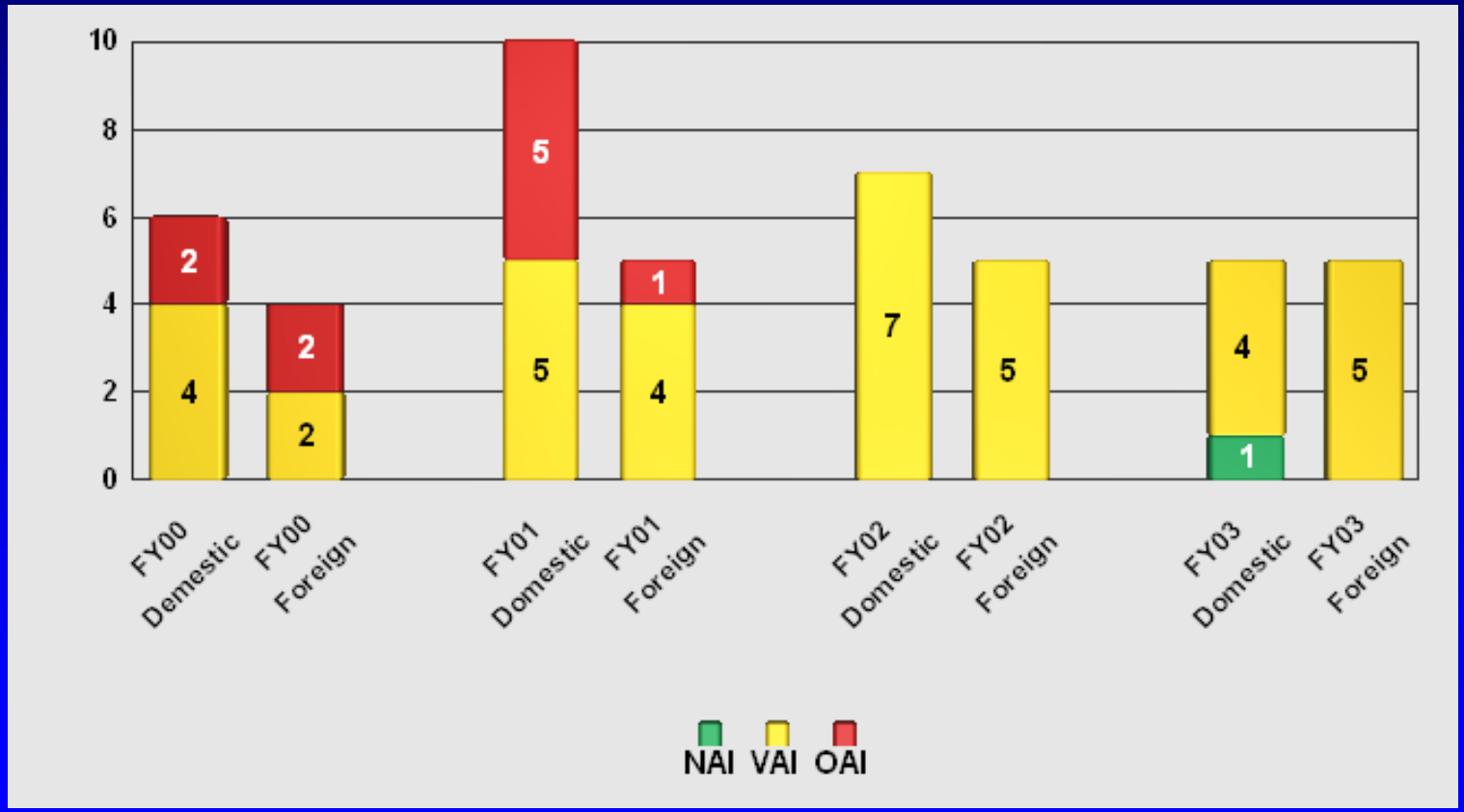
FDA Inspection Classification System

- **NAI - No Action Indicated**
- **VAI - Voluntary Action Indicated**
- **OAI - Official Action Indicated**

Fractionator Inspection Classifications



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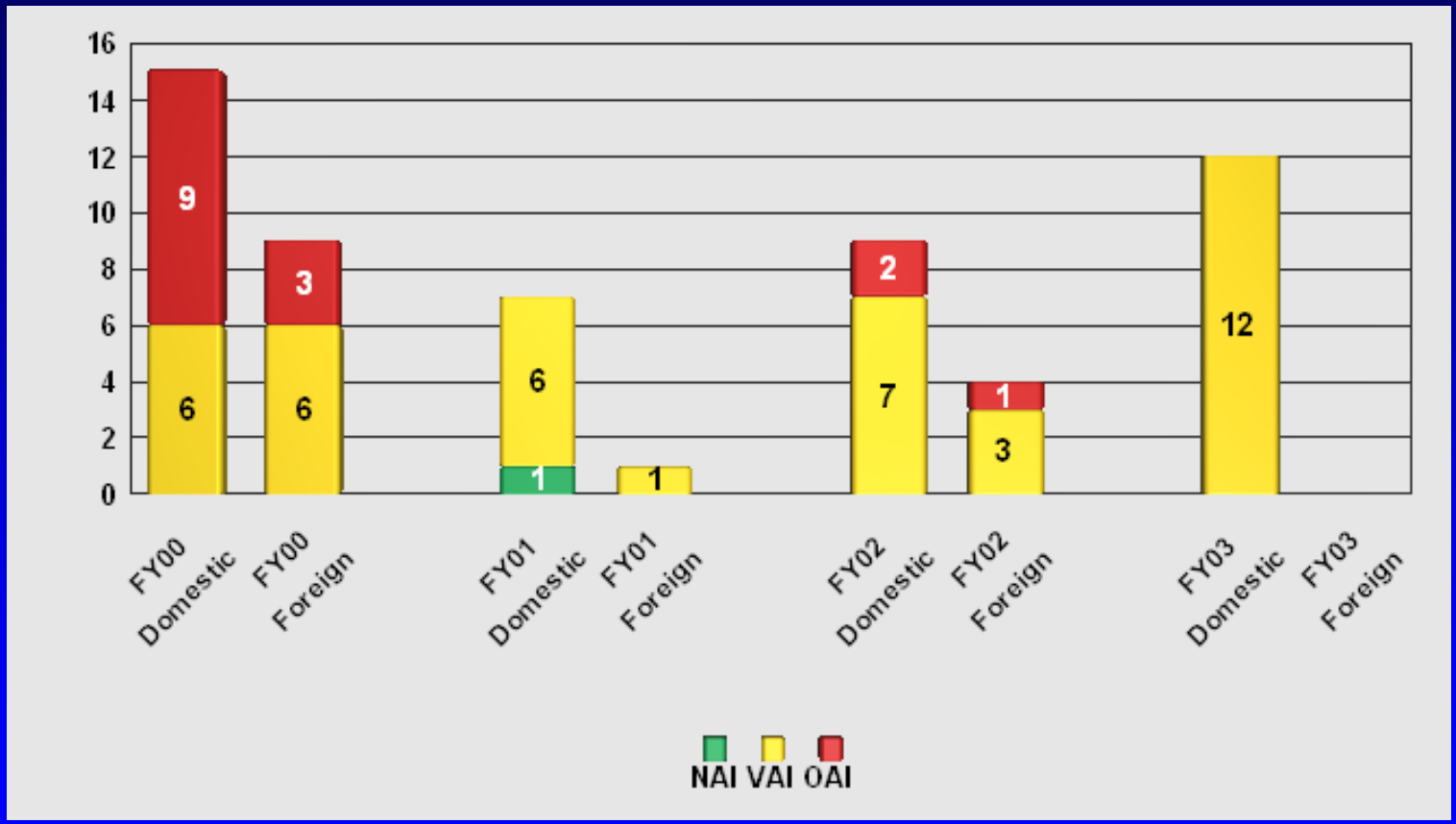
Device Inspection Classifications



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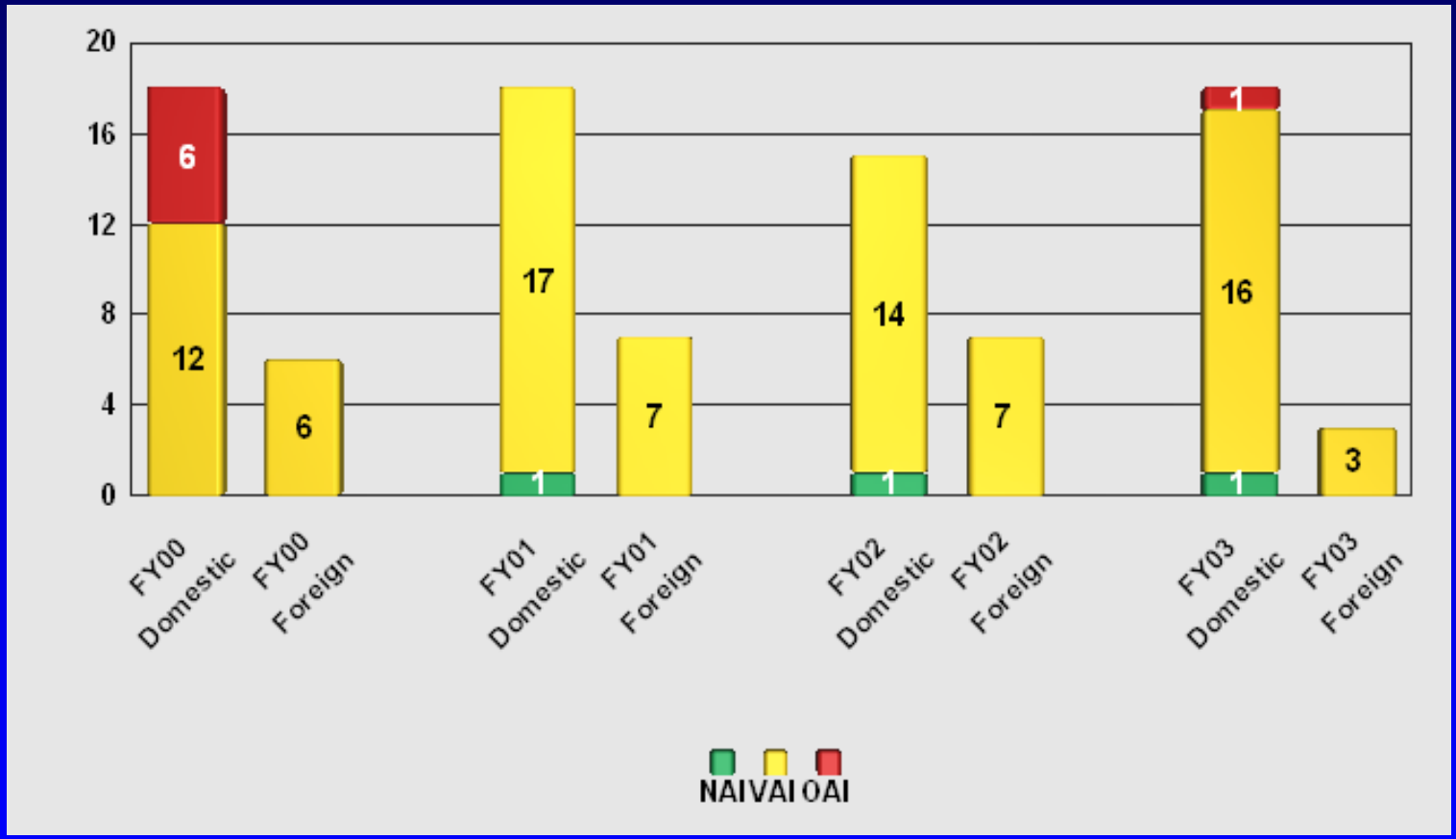
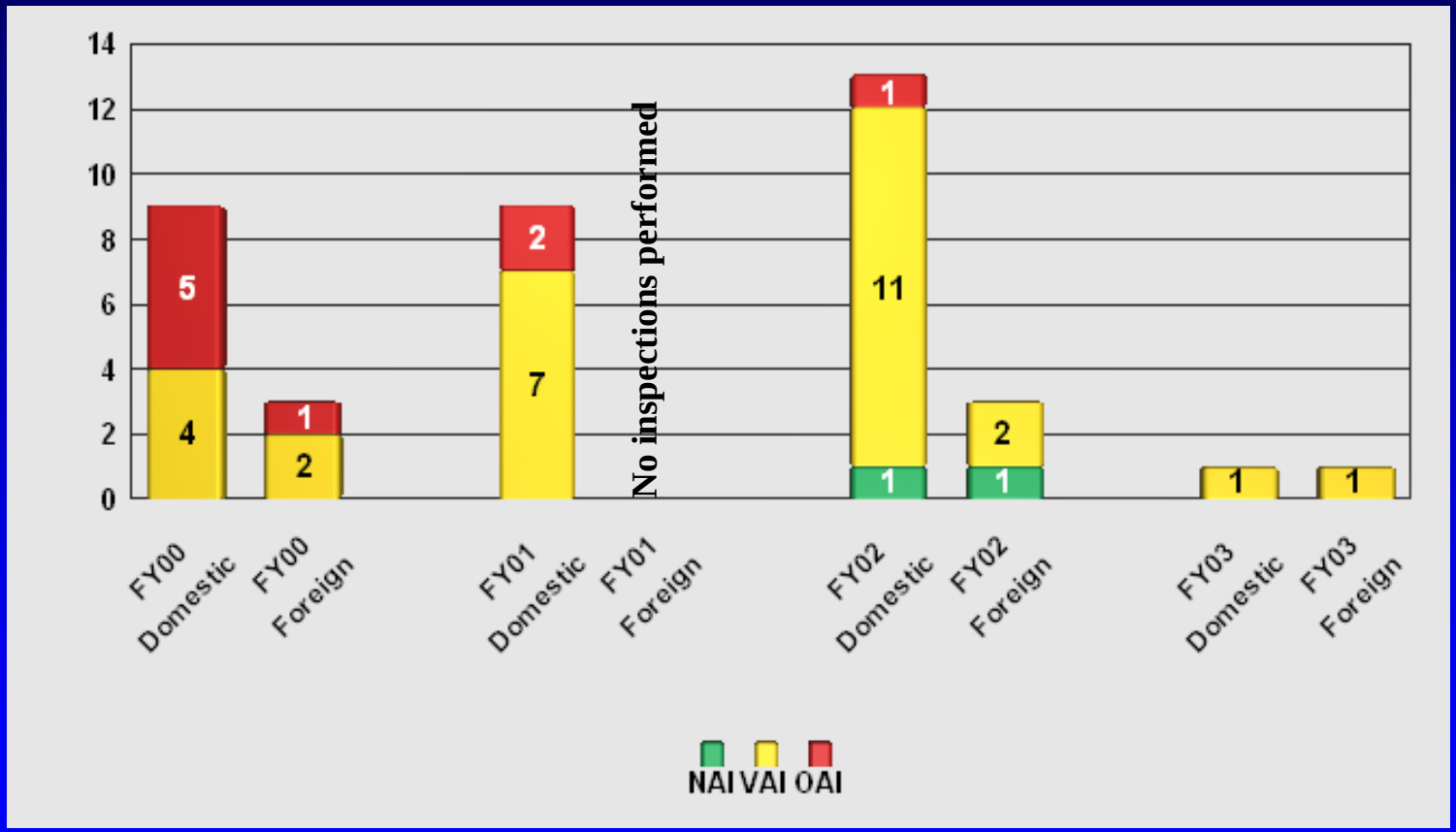
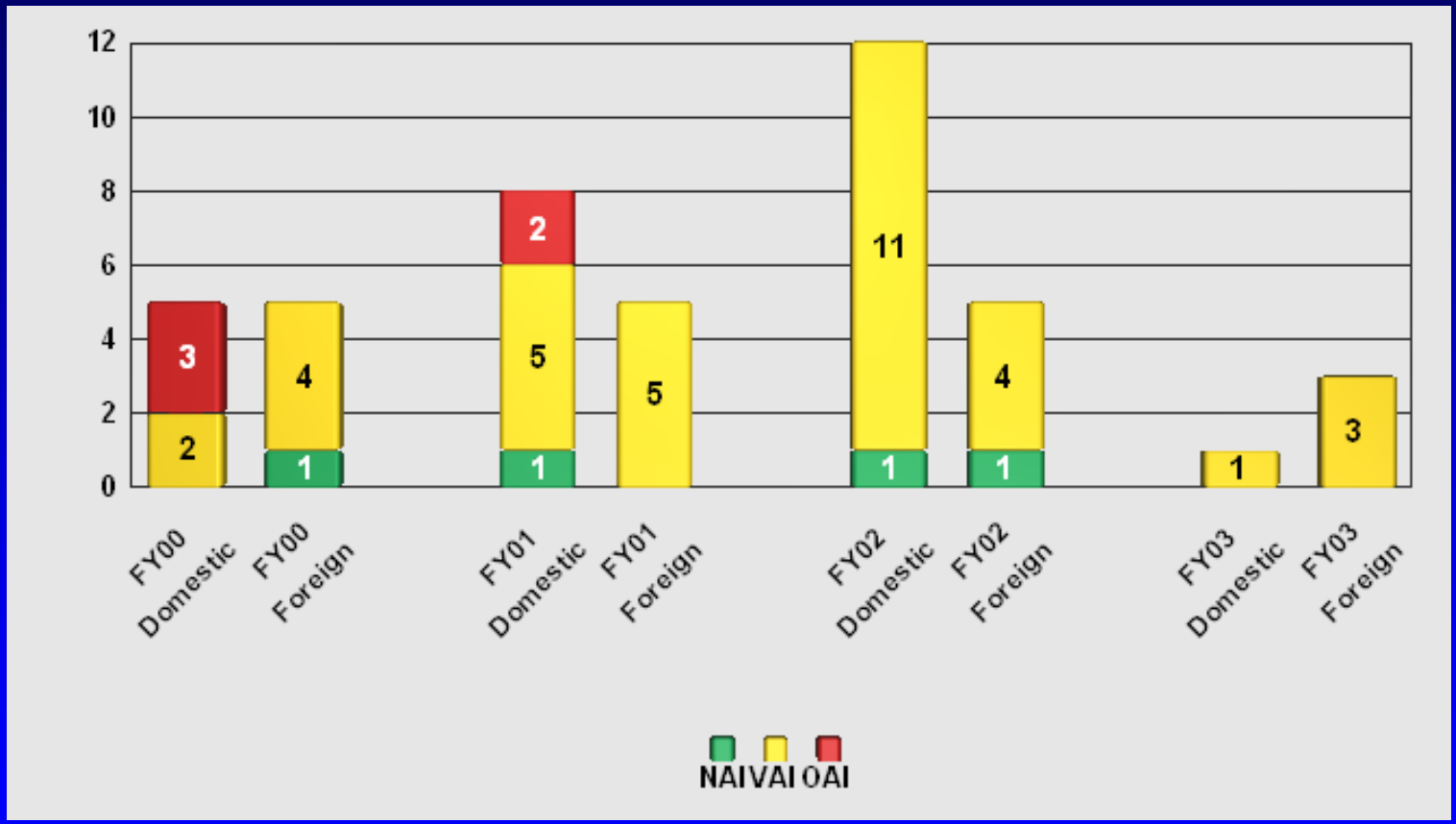
Therapeutic Inspection Classifications



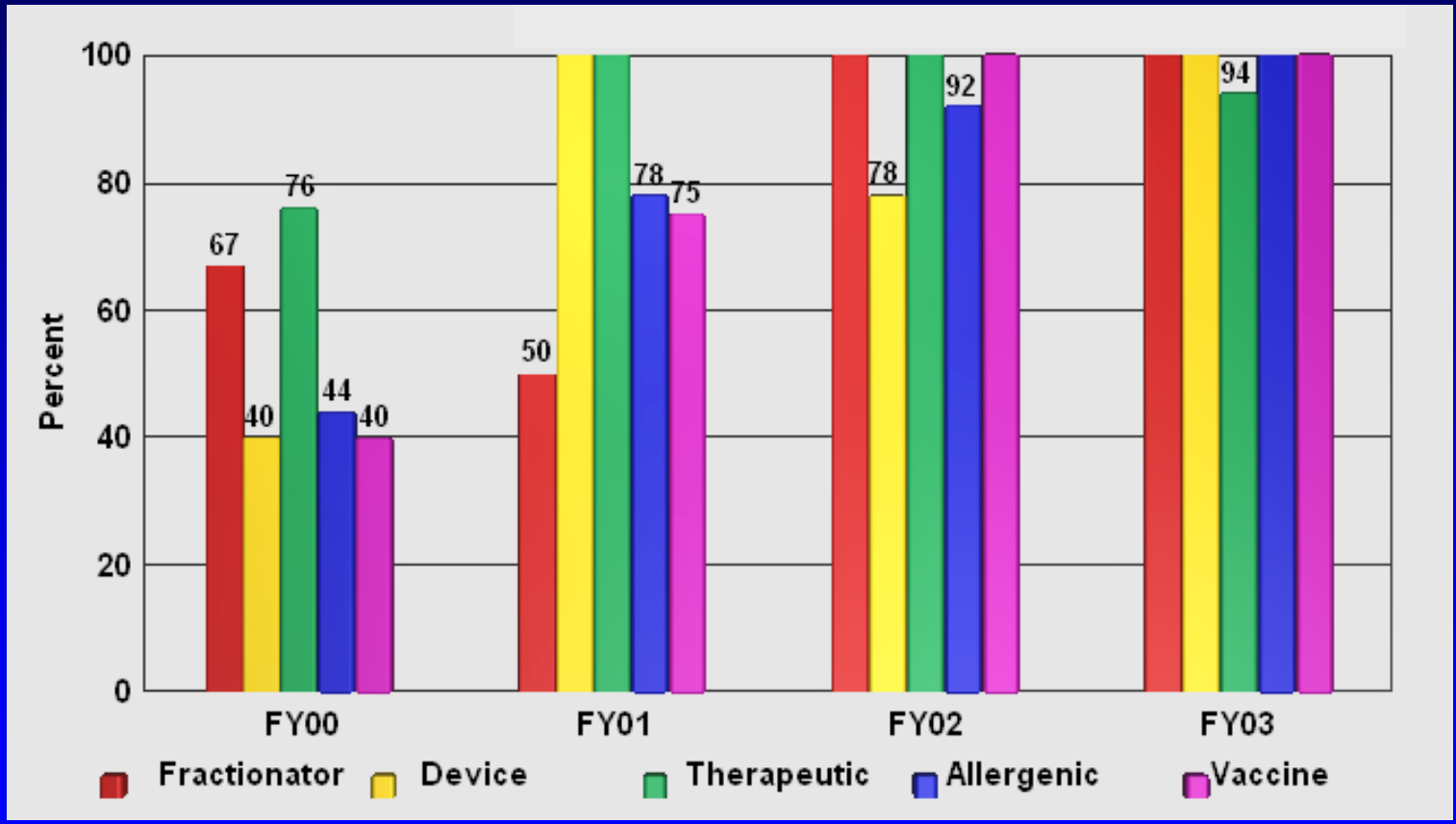
Allergenic Inspection Classifications



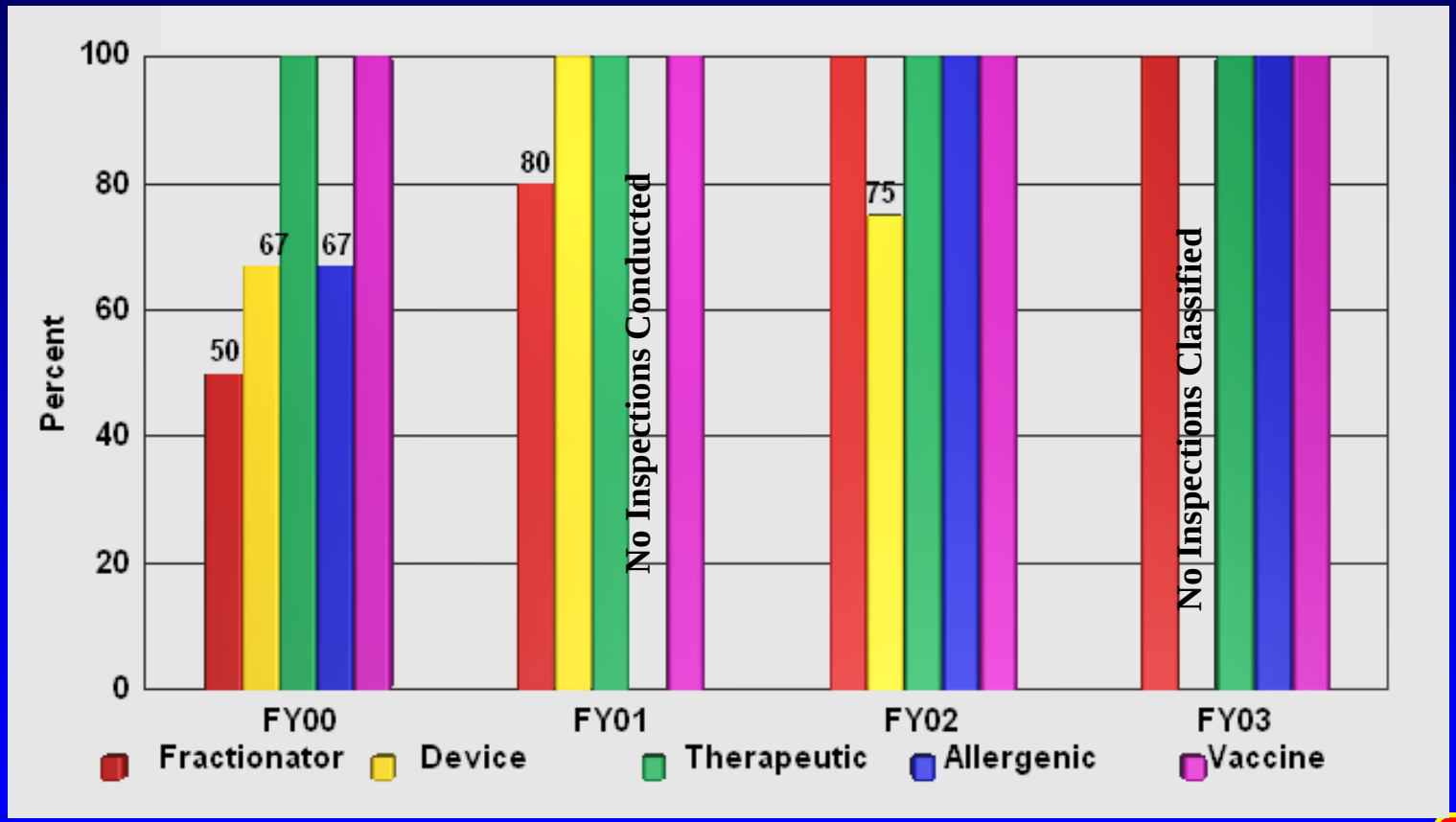
Vaccine Inspection Classifications



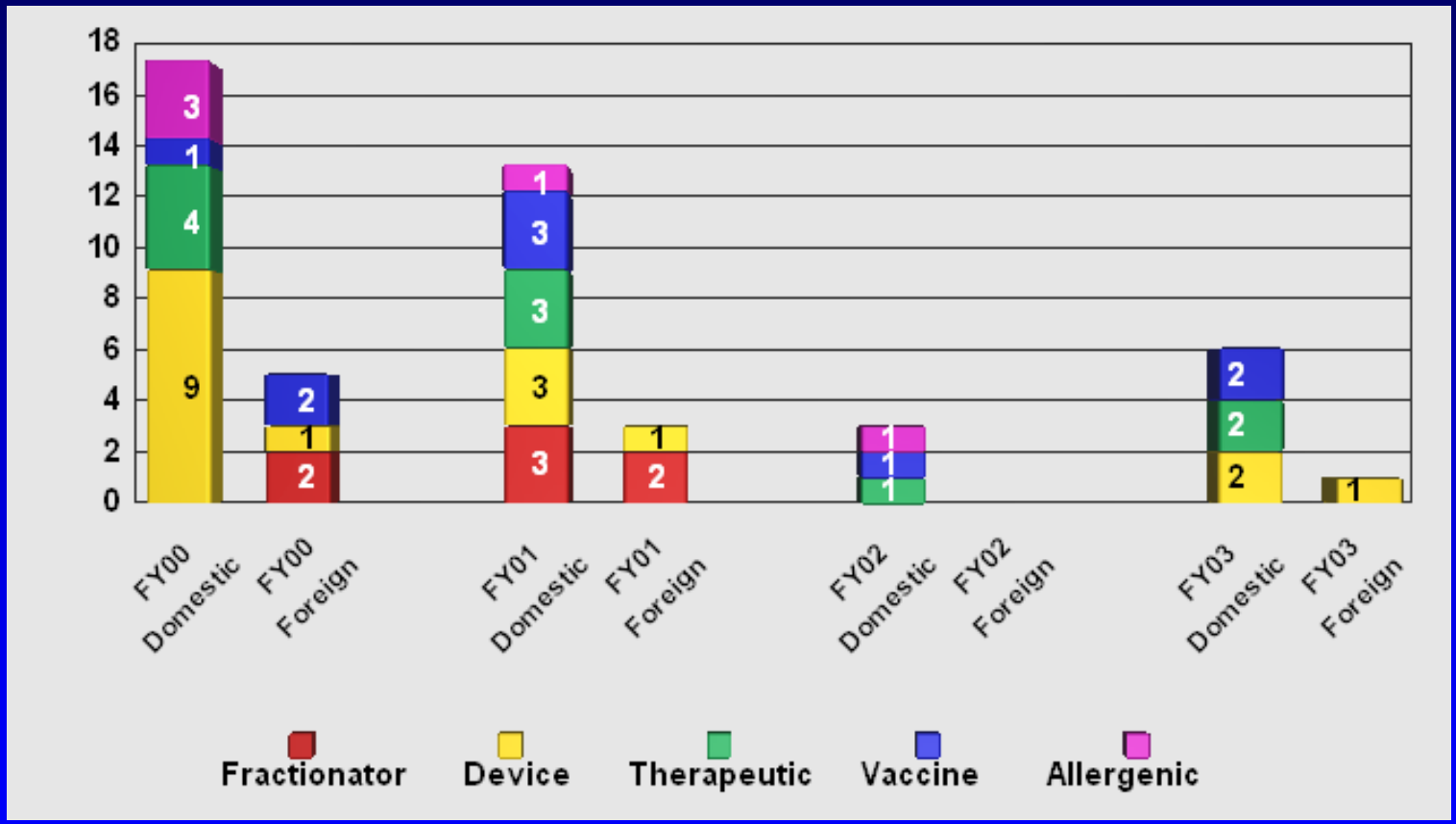
NAI/VAI Rate
Domestic



NAI/VAI Rate
Foreign



Warning Letters



Not limited to CGMP

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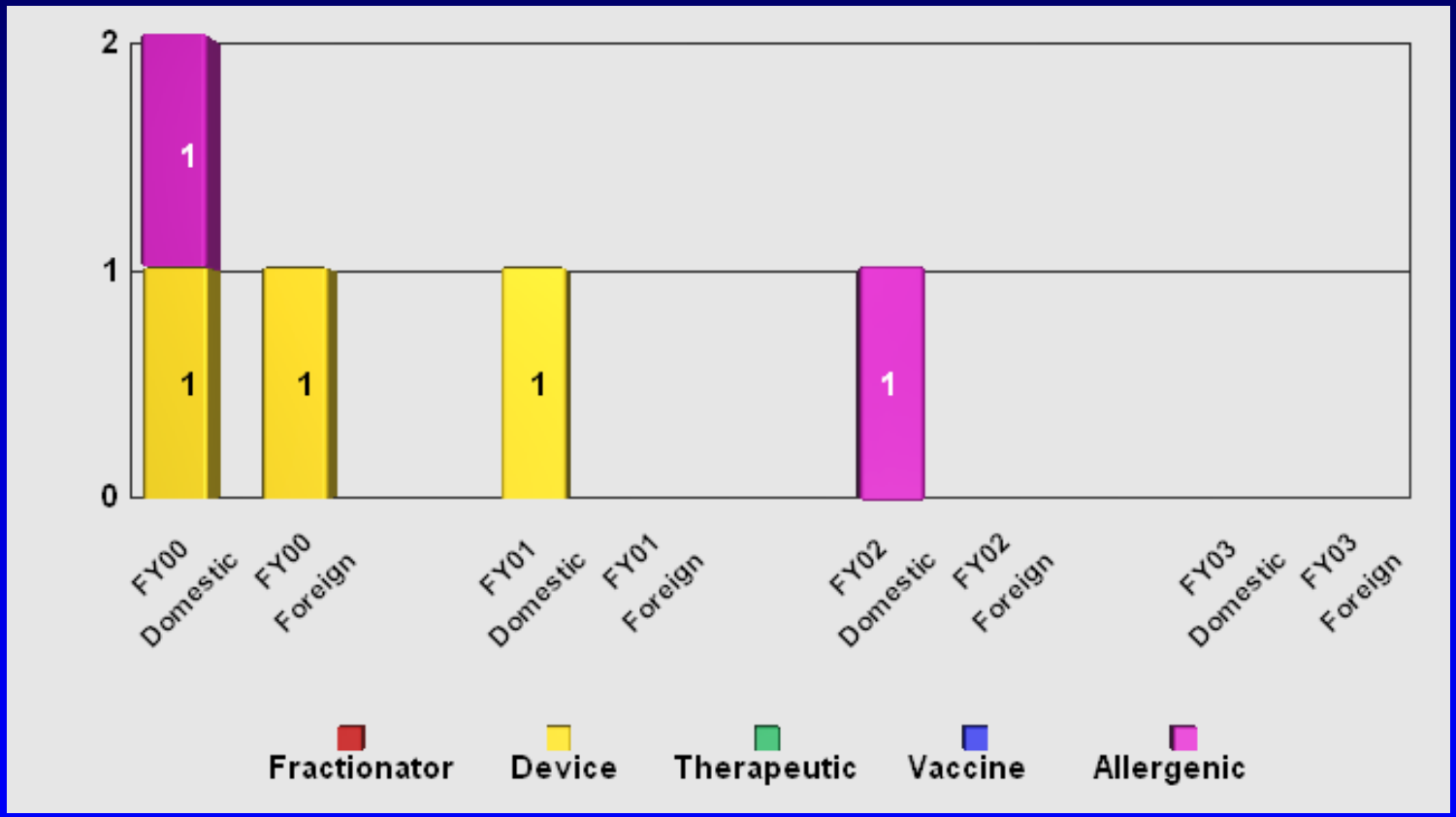
Notice of Intent to Revoke



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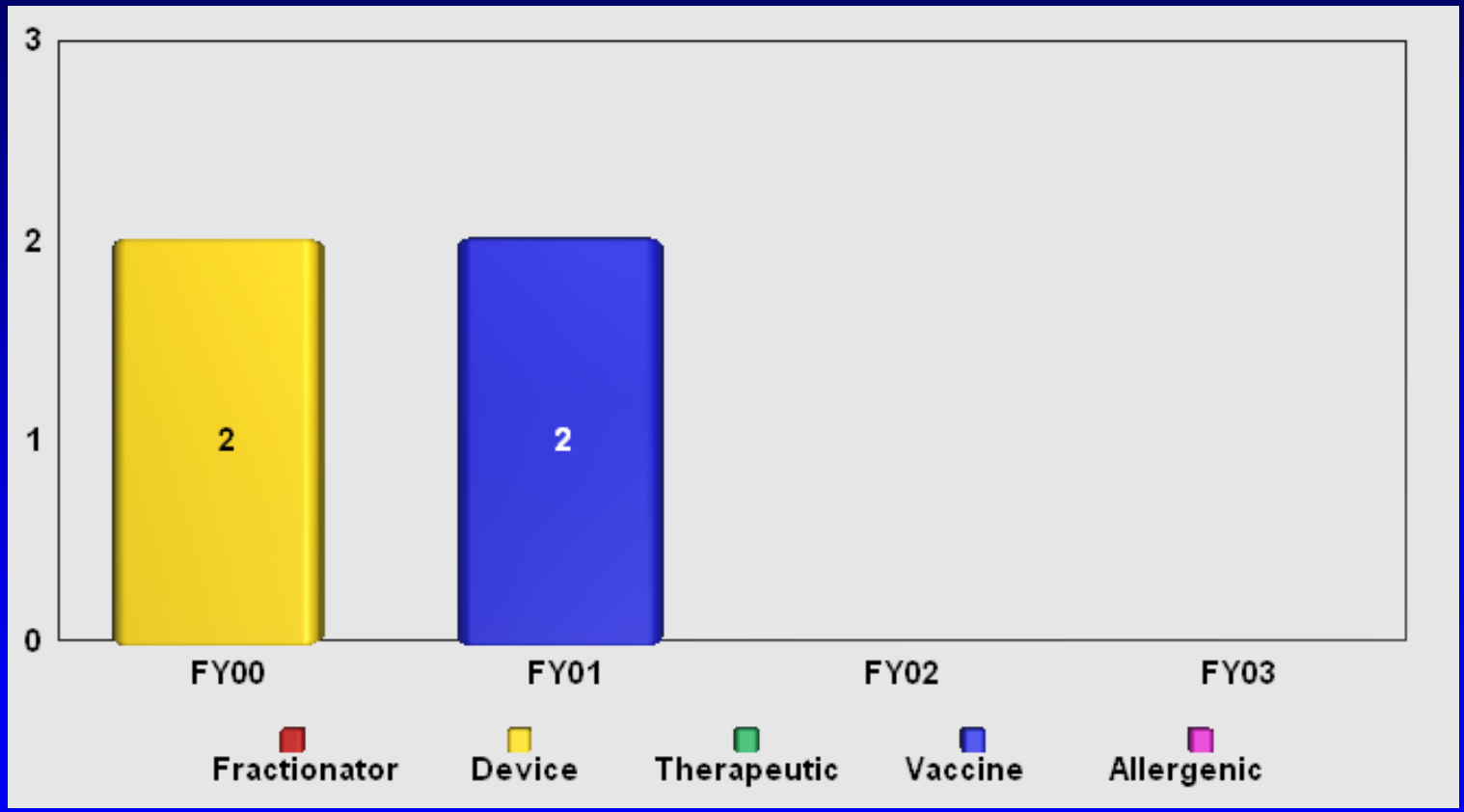
Injunctions



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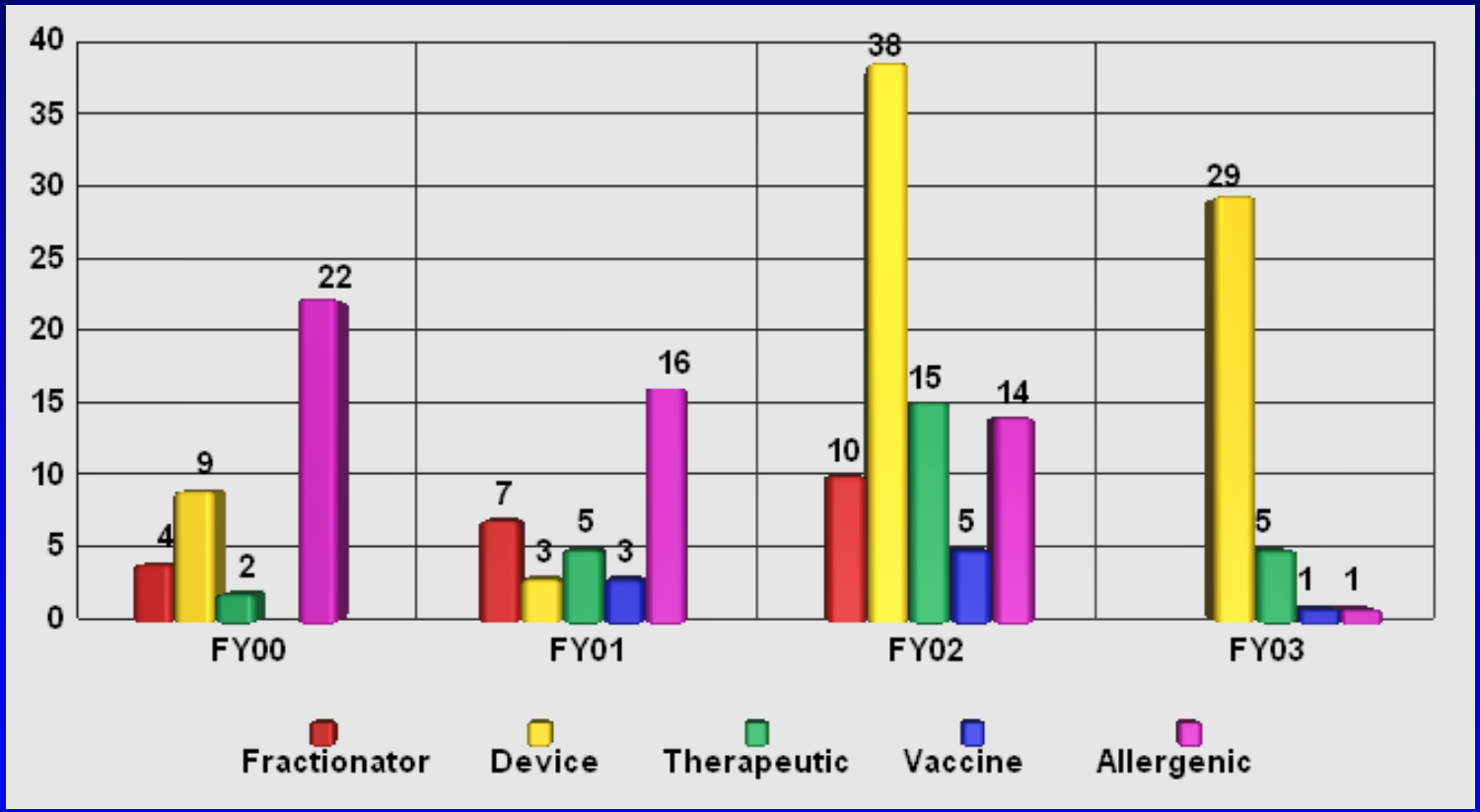
Recalls Classified



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Device Recalls FY02-03

Primary Reasons – Devices and IVDs

- Software defects
- Potency/test results
- Antigen labeling incorrect
- Bacterial contamination
- Leaking collection sets

Import Alert

- Information to FDA district offices concerning unusual or new problems
- Provides background and compliance guidance information
- Available in FDA's Import Alert Retrieval System (FIARS)
  - http://www.fda.gov/ora/fiars/ora_import_alerts.html
- Provides guidance regarding automatic detentions (if applicable)

What Does Detention Mean To You?

- **Inability to export product to U.S.**
- **Impact on trade/contractual obligations**

Importer Options

- **Appeal the detention**
  - Submit private laboratory report of analysis
  - Provide certification of product where applicable
  - Render other than a regulated product
- **Request refusal of admission**
  - Exportation or destruction

Importer Options
continued

- **Request consideration for bringing article into compliance by reconditioning**
  - **e.g., relabeling**

Bioresearch Monitoring

- **Routine inspections**
  - **Referrals/complaints/surveillance/ submission of BLA**
- **Emphasis on patient safety**
- **Ensure quality and integrity of data**

Counterfeiting/Tampering

- **Substantial increase in counterfeiting nationally and internationally in recent years**
- **CBER performs dual role**
  - **Safety**
  - **Availability**
- **Collaboration with FDA's Office of Criminal Investigations (OCI)**

Counterfeiting/Tampering (continued)

- First priority is to provide consumers timely and relevant information relating to safety and quality
- Related priorities are to investigate scope of event, assure removal from market, and investigate counterfeiters
- Sources of information include:
  - Surveillance
  - Consumers
  - Industry
  - Other FDA components
  - Other Government agencies

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FDA's Counterfeit Drug Initiative

- **Announced July 16, 2003**
- **Designed to:**
  - **Better identify the risks and threats from counterfeit drugs**
  - **Establish a public and private coalition to fight drug counterfeiting and distribution**
  - **Develop new tools to aid in identifying, deterring, and combating counterfeiting**

FDA's Counterfeit Drug Initiative
continued

- **Internal FDA task force is working to:**
  - Develop strategic plan to decrease risk of counterfeits entering U.S. marketplace
  - Strengthen FDA's collaborative relationships with other Federal agencies
  - Identify mechanisms for strengthening nation's protections against counterfeiting
  - Assess the extent to which new technologies can help assure authenticity of products

Final Report

- Issued February 18, 2004
- Pharmaceutical industry should adopt secure business practices
- States should adopt and enforce stronger anti-counterfeiting requirements
- New technologies should be employed
  - Radiofrequency identification technology (RFID)
  - Authentication technologies

Final Report
(continued)

- **Electronic pedigree (RFID) should accomplish and surpass goals of Prescription Drug Marketing Act**
  - **FDA intends to focus on tracing movement of drugs**
- **Congress should increase criminal penalties and strengthen FDA's authority**
- **FDA intends to develop effective reporting and rapid response systems, including dissemination of information to public**

Reasons for Increase in Counterfeiting

- **Better technology available to counterfeiters**
- **Increasing sophistication of counterfeiting operations**
- **Online sale of prescription drugs**
- **Increased international commerce**
- **Weak spots in domestic wholesale drug distribution chain**

Risks from Counterfeits

- Subpotent or superpotent ingredients
- No active ingredients
- Ineffective treatments
- Infections or other potential detrimental health effects

Aggressive Enforcement Strategy

- FDA initiated 73 counterfeit drug investigations between October 1996 and June 2003, with a substantial increase between 2001 and the present
- Resulted in 44 arrests and 27 convictions
- Criminal investigations ongoing
- Fines and/or restitution have been imposed in excess of $250,000

Counterfeiting of Biologics
Recent Examples

- **Neupogen®**
  - **Manufactured by Amgen, Inc.**
  - **Used to stimulate white blood cell production in patients undergoing chemotherapy**
  - **May 2001 - vials containing clear liquid but no active ingredient**

Counterfeiting of Biologics

Recent Examples - continued

- **Epogen®**
  - **Manufactured by Amgen**
  - **Used to stimulate production of red blood cells as treatment for anemia associated with chronic renal failure for patients on dialysis**
  - **May 2002 – vials containing clear liquid but active ingredient 20 times lower than expected**

Counterfeiting of Biologics

Recent Example (continued)

- **Procrit®**
  - Manufactured by Amgen
  - Distributed by Ortho Biotech Products
  - Used to stimulate production of red blood cells as treatment for anemia associated with chemotherapy, HIV therapy, kidney disease, etc.
  - April 2003 – Expired vials containing clear liquid but active ingredient 20 times lower than expected
  - March 2003 – Vials containing no active ingredient but clear liquid contaminated with bacteria
  - June 2002 - Vials containing clear liquid but active ingredient 20 times lower than expected

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Counterfeiting-Related Arrests

- **Counterfeit Procrit®**
  - **Three people arrested in Miami in February 2003**
  - **All pled guilty on June 11, 2003**
    - **Trafficking in counterfeit goods**
    - **Unlawful distribution of prescription drugs without a license**
  - **Two sentenced to prison, one to house arrest**

Counterfeit-Related Indictments

- 19 people indicted by Florida grand jury on July 22, 2003
- Involved Neupogen®, Gammagard®, Epogen®, and Lipitor®
- Charges vary by individual and include:
  - Racketeering
  - Conspiracy to commit racketeering
  - Organized scheme to defraud
  - Sale or delivery of a controlled substance
  - Possession with intent to sell prescription drugs
  - Purchase or receipt of a prescription drug from unauthorized person

Industry's Efforts

- Individual firms working on ways to deter/prevent counterfeiting
- Pharmaceutical Research and Manufacturers of America (PhRMA)
  - Five-point program to combat counterfeits
- Healthcare and Distribution Management Association (HDMA)
- Others
- Will be engaged as part of FDA Initiative

We're Here to Help You!

WWW.FDA.GOV/CBER

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  - **Consumers, health care professionals:**
    octma@cber.fda.gov
- **Phone:**
  - **301-827-1800**